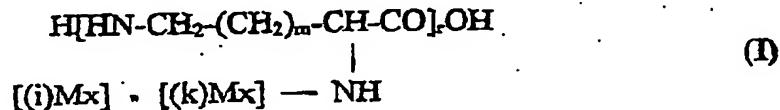


ART 34 AMDT

23

1) Polycation bioconjugates characterized in that each of them contains isopolypeptide polycation carrier molecules having free α -amino groups, and these carrier molecules are conjugated by chemical bonds with suitably selected molecules which may either be identical ones or of (two or more i.e. "x") different kind, bearing functional groups appropriate for conjugation, and the polycation bioconjugates synthetized this way can be described by the general formula (I):



wherein:

"r" designates the number of diamino-monocarbonic acyl group monomers which is between 20 and 400 as a mean value.

"m" = 0, 1, 2, 3, ... k,

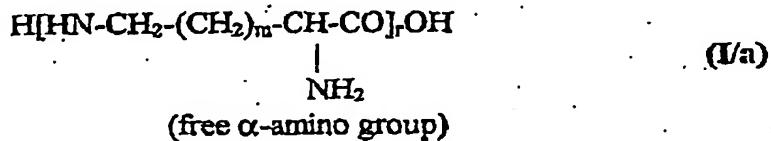
"[(k)Mx]" designates enhancer molecules and/or connecting molecules conjugated by covalent (= k) bonds to the isopolypeptide polycation carrier molecule, and

"[(i)Mx]" designates enhancer molecules conjugated by ionic (=i) bonds to the isopolypeptide polycation carrier molecule, whereas the said enhancer molecules and connecting molecules having appropriate functional groups for conjugation may either be identical ones or of (two or more i.e. "x") different kind, and the enhancer molecules can be conjugated:

- directly and/or
- indirectly through a connecting molecule,

and further the joint occurrence of $[(k)Mx]$ and $[(i)Mx]$ within the same polycation bioconjugate is symbolized by $[(k/i)Mx]$.

2) Polycation bioconjugates of general formula (I), prepared according to Claim 1, characterized in that the isopolypeptide polycation carrier molecules, which are included in each of polycation bioconjugates, synthetized from diamino-monocarbonic acyl group monomers, are of the same configuration (i.e. either D-, or L-), and the individual monomers are not linked together by their amino groups in the α -positions, but by those in other (i.e. in β -, γ -, δ -, s...etc.) positions - according to the value of "m", and thus the isopolypeptide polycation carrier molecules (further on: carrier molecules), having free α -amino groups, are of general formula (II/a):



wherein

"r" and "m" have the same meaning as in general formula (I).

3) Polycation bioconjugates of general formula (I), prepared according to Claim 1, characterized in that suitably selected $[(k)Mx]$ and/or $[(i)Mx]$ molecules, which may either be identical ones or of (two or more i.e. "x") different kind, are conjugated to a given representative of carrier molecules of general formula (II/a), by covalent and/or ionic bonds.

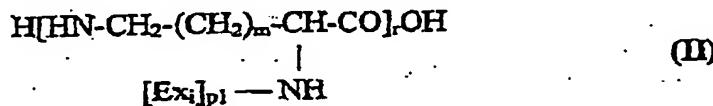
ART 34 AMENDMENT

4) Polycation bioconjugates of general formula (I), according to Claim 3, characterized in that the conjugation of the $[(k)Mx]$ and/or $[(i)Mx]$ molecules to a given representative of carrier molecules of general formula (I/a), by covalent and/or ionic bonds takes place directly and/or indirectly in a definite ratio, preferably to reach a saturation of 10 to 100 %.

5) Polycation bioconjugates of general formula (I), prepared according to Claim 1, characterized in that they include those bioconjugates in which a given representative of carrier molecules of general formula (I/a) is directly conjugated by covalent bonds with $[Ex_i]$ enhancer molecules, which may either be identical ones or of (two or more i.e. "x") different kind, and in these bioconjugates:

$$[(k)Mx] = [Ex_i]_{p1},$$

and the polycation bioconjugates are being described by the general formula (II):



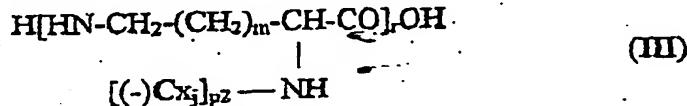
wherein:

"Ex" in $[Ex_i]_{p1}$ designates the Ex enhancer molecules of different ("x") kind conjugated directly to a given representative of carrier molecules of general formula (I/a) by covalent bonds, and
 "i" indicates whether the Ex enhancer molecules, conjugated to the given carrier molecule by covalent bonds, are identical ones ($i = 1$), or they are of different kind according to the number "i" ($i = 2, 3, \dots, x$), and
 "p1" indicates a degree of saturation in % of a carrier molecule of general formula (I/a) with $[Ex_i]$ enhancer molecules, the value of which is > 0 and ≤ 100 , whereby the ratio between the free (not involved in chemical bonds) and bound NH_2 -groups is determined, which in turn influences the charge and the cationic character of the polycation bioconjugates, and
 "r" and "m" have the same meaning as in general formula (I).

6) Carrier molecules of general formula (I/a), prepared according to Claim 2, characterized in that a given representative of them are conjugated by covalent bonds with $[(-)Cx_j]$ connecting molecules of anionic character, which may either be identical ones or of (two or more i.e. "x") different kind, and the connecting molecules are suitably chosen dicarbonic acids, tricarbonic acids, carbohydrates, or amino acids, or peptide chain elongators, and in these compounds:

$$[(k)Mx] = [(-)Cx_j]_{p2}$$

and the conjugates are being described by the general formula (III):



ART 34 AND

wherein:

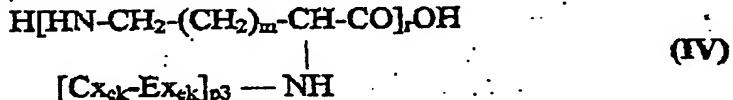
" $(-)$ Cx" in $[(-)Cx_j]_{p_2}$ designates $(-)Cx$ connecting molecules of exclusively anionic character of different ("x") kind linked to a given representative of carrier molecules of general formula (I/a) by covalent bonds, and
 "j" indicates whether the $(-)Cx$ connecting molecules, conjugated to the given carrier molecule by covalent bonds, are identical ones ($j = 1$), or they are of different kind according to the number "j" ($j = 2, 3, \dots, x$), and
 " p_2 " indicates a degree of saturation in % of a carrier molecule of general formula (I/a) by $[(-)Cx_j]$ connecting molecules of exclusively anionic character, the value of which is > 0 and ≤ 100 , whereby the ratio between the free (not involved in chemical bonds) and bound NH_2 - groups is determined, which in turn influences the charge and the cationic character of the polycation bioconjugates, and
 "r" and "m" have the same meaning as in general formula (I).

7) Conjugates of general formula (III), according to Claim 6, characterized in that the carrier molecules of general formula (I/a) of cationic character, due to conjugation of the $[(-)Cx_j]$ connecting molecules of anionic character to them by covalent bonds, become capable of building up such polycation bioconjugates, in which additional possibilities arise to establish ionic bonds with enhancer molecules of cationic character.

8) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they include those bioconjugates in which a given representative of carrier molecules of general formula (I/a) is indirectly conjugated with $[Ex_k]$ enhancer molecules, which may either be identical ones or of (two or more i.e. "x") different kind, through $[Cx_{ck}]$ connecting molecules, which may also be either identical ones or of (two or more i.e. "x") different kind, and in these bioconjugates both of the chemical bonds between the carrier molecule and $[Cx_{ck}]$, as well as between the $[Cx_{ck}]$ and $[Ex_k]$ are covalent ones, and in these bioconjugates:

$$[(k)Mx] = [Cx_{ck}-Ex_k]_{p_3},$$

and the polycation bioconjugates are being described by the general formula (IV):



wherein:

"Cx-Ex" in $[Cx_{ck}-Ex_k]_{p_3}$ designates the Ex enhancer molecules of different ("x") kind, conjugated by covalent bonds indirectly, through Cx connecting molecules of different ("x") kind, that are also conjugated by covalent bonds to a given representative of carrier molecules of general formula (I/a), and
 "ck" indicates whether the Cx connecting molecules, conjugated to the given carrier molecule by covalent bonds, are identical ones ($ck = 1$), or they are of different kind according to the number "ck" ($ck = 2, 3, \dots, x$), and
 "ek" indicates whether the Ex enhancer molecules, conjugated to the given carrier molecule indirectly through Cx connecting molecules by covalent bonds, are identical ones ($ek = 1$), or they are of different kind according to the number "ek" ($ek = 2, 3, \dots, x$),
 " p_3 " means a degree of saturation in % of a carrier molecule by $[Ex_k]$ enhancer molecules coupled to $[Cx_{ck}]$ connecting molecules, the value of which is > 0 and ≤ 100 , whereby the

ART 34 AMDT

ratio between the free (not involved in chemical bonds) and bound NH₂-groups is determined, which in turn influences the charge and the cationic character of the polycation bioconjugates, and further "r" and "m" have the same meaning as in general formula (I).

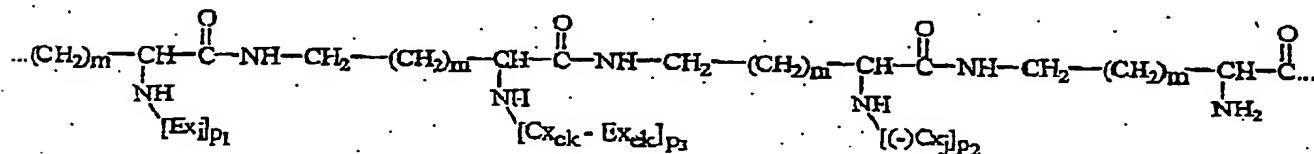
9) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they include those bioconjugates in which to a given representative of carrier molecules of general formula (IVa), are conjugated by covalent bonds

- a/ [Ex_i] enhancer molecules and/or
- b/ [(-)Cx_j] connecting molecules of anionic character and/or
- c/ [Cx_{ek}-Ex_{ek}] indirectly coupled enhancer molecules

which may either be identical ones or of (two or more i.e. "x") different kind, with the proviso, that from among the [Ex_i] and/or [(-)Cx_j] and/or [Cx_{ek}-Ex_{ek}] types of molecules at least two are contained in the bioconjugate, and in these bioconjugates:

$$\begin{aligned} [(k)Mx] = & [Ex_i]_{p1} + [(-)Cx_j]_{p2}, \text{ or} \\ & [Ex_i]_{p1} + [Cx_{ek}-Ex_{ek}]_{p3}, \text{ or} \\ & [Cx_{ek}-Ex_{ek}]_{p3} + [(-)Cx_j]_{p2}, \text{ or} \\ & [Ex_i]_{p1} + [Cx_{ek}-Ex_{ek}]_{p3} + [(-)Cx_j]_{p2}, \end{aligned}$$

and the polycation bioconjugates are being described by the schematic formula (V):



(V)

wherein:

- "[Ex_i]_{p1}" has the same meaning as in general formula (II),
- "[(-)Cx_j]_{p2}" has the same meaning as in general formula (III),
- "[Cx_{ek}-Ex_{ek}]_{p3}" has the same meaning as in general formula (IV),

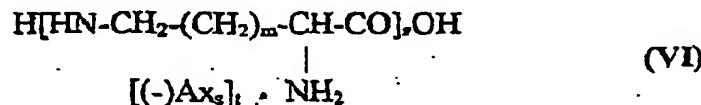
"m" has the same meaning as in general formula (I), further the value of "p₁"+"p₂"+"p₃" > 0 and ≤ 100, and from among "p₁", "p₂" and "p₃" the value of at least two are greater than 0; further in a given polycation bioconjugate the Ex molecules in [Ex_i], and the (-)Cx molecules in [(-)Cx_j] are not necessarily identical with those Ex and Cx molecules occurring in [Cx_{ek}-Ex_{ek}], which divergence is symbolized by "x".

10) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they include those bioconjugates in which a given representative of carrier molecules of general formula (IVa) is directly conjugated, exclusively by ionic bonds with [(-)Ax_e] enhancer molecules of anionic character, which may either be identical ones or of (two or more i.e. "x") different kind, and in these bioconjugates

$$[(i)Mx] = [(-)Ax_e].$$

ART 34 AMDX

and the polycation bioconjugates so obtained can be described by the general formula (VI):



wherein:

- "(-)Ax" in $[(-)\text{Ax}_s]$, designates those $(-)Ax$ enhancer molecules of anionic character, which may either be identical ones or of (two or more i.e. "x") different kind, that are conjugated to a given representative of carrier molecules of general formula (I/a) by ionic bonds, and
- "s" indicates whether the anionic/polyanionic molecules, conjugated to the given carrier molecule by ionic bonds, are identical ones ($s = 1$), or, they are of different kind according to the number "s" ($s = 2, 3, \dots, x$), and
- "z" means a degree of saturation in % of the given representative of carrier molecules of general formula (I/a) by $[(-)\text{Ax}_s]$ anions, the value of which is > 0 and ≤ 100 , whereby the ratio between the free (not involved in chemical bonds) and bound NH_2 -groups is determined, which in turn influences the charge and the cationic character of the polycation bioconjugates, and
- "r" and "m" have the same meaning as in general formula (I).

11) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they include conjugates of general formula (III), prepared according to Claim 6, and these are conjugated with $[(+)\text{Kx}_u]$ enhancer molecules of cationic character, which may either be identical ones or of (two or more i.e. "x") different kind, by ionic bonds via the $[(-)\text{Cx}_j]$ connecting molecules of anionic character, and in these bioconjugates



and the polycation bioconjugates are being described by the general formula (VII):

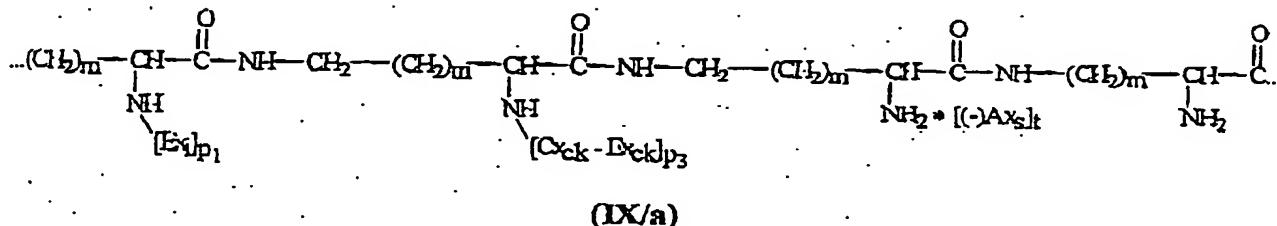


wherein:

- " $(+)\text{Kx}$ " in $[(+)\text{Kx}_u]_z$ designates the $(+)\text{Kx}$ enhancer molecules of cationic character, which may either be identical ones or of (two or more i.e. "x") different kind, that are conjugated to a given representative of conjugates of general formula (III), and
- "u" indicates whether the cationic/polycationic molecules linked to the given conjugate of general formula (III) by ionic bonds, are identical ones ($u = 1$), or they are of different kind according to the number "u" ($u = 2, 3, \dots, x$), and
- "z" means a degree of saturation in % of the given representative of conjugates of general formula (III) by $[(+)\text{Kx}_u]$ cations, the value of which is > 0 and ≤ 100 , whereby the ratio between the free (not involved in chemical bonds) and bound NH_2 -groups is determined, which in turn influences the charge and the cationic character of the polycation bioconjugates, and as the $[(+)\text{Kx}_u]$ molecules of cationic character can exclusively be

ART 34 AMDT

29



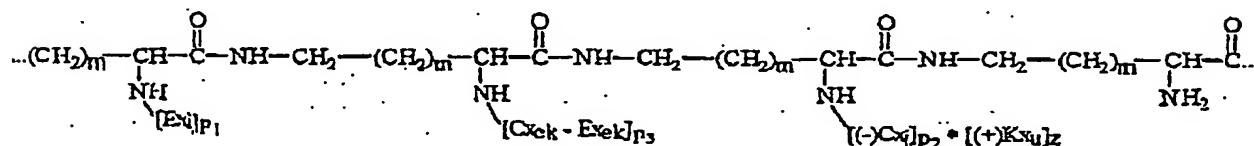
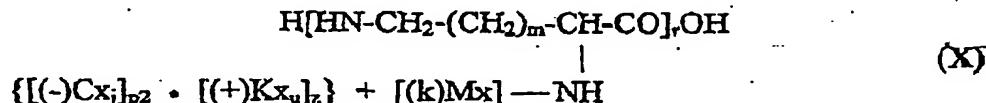
wherein:

- "[(-)\text{Ax}_s]_t"
- "[\text{Ex}_i]_{p1}" has the same meaning as in general formula (VI),
- "[\text{Cx}_{ck} - \text{Ex}_{ck}]_{p3}" has the same meaning as in general formula (II),
- "[(k)\text{Mx}]", "m", "r" have the same meaning as in general formula (I), further
- "p₁" + "p₃" + "t" > 0 and ≤ 100, and from among
- "p₁" and "p₃" the value of at least one > 0; and
- "t" > 0.

14) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they include polycation bioconjugates of schematic formula (V), prepared according to Claim 9, in which there are $[(\text{-})\text{Cx}_j]$ connecting molecules of anionic character which may either be identical ones or of two or more "x" different kind, and these are conjugated with $[(+)\text{Kx}_u]$ enhancer molecules of cationic character which may either be identical ones or of (two or more i.e. "x") different kind, by ionic bonds, and in these bioconjugates

$$[(k/i)\text{Mx}] = [\text{Ex}_i]_{p1} + \quad \{[(-)\text{Cx}_j]_{p2} \cdot [(+)\text{Kx}_u]_z\} \text{ or} \\ [\text{Cx}_{ck} - \text{Ex}_{ck}]_{p3} + \quad \{[(-)\text{Cx}_j]_{p2} \cdot [(+)\text{Kx}_u]_z\}, \text{ or} \\ [\text{Ex}_i]_{p1} + [\text{Cx}_{ck} - \text{Ex}_{ck}]_{p3} + \quad \{[(-)\text{Cx}_j]_{p2} \cdot [(+)\text{Kx}_u]_z\}$$

and the polycation bioconjugates are being described by the general formula (X), or by the schematic formula (X/a):



(X/a)

wherein:

- "[(-)\text{Cx}_j]_{p2} \cdot [(+)\text{Kx}_u]_z"
- "[\text{Ex}_i]_{p1}" has the same meaning as in general formula (VII),
- "[\text{Cx}_{ck} - \text{Ex}_{ck}]_{p3}" has the same meaning as in general formula (II),
- "[(k/i)\text{Mx}]", "m", "r" have the same meaning as in general formula (I), further

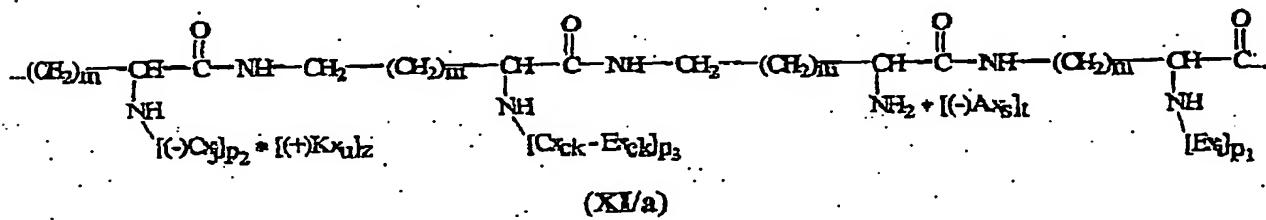
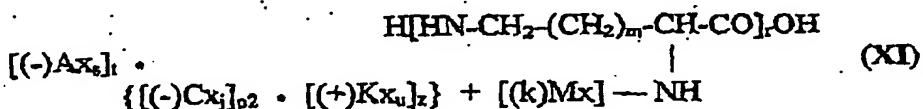
30

" p_1 " + " p_3 " + "z" > 0 and ≤ 100 , and from among
 " p_1 " and " p_3 " the value of at least one > 0; and
 "z" = " p_2 " > 0.

15) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they include those bioconjugates in which to the free α -amino groups of a given representative of polycation bioconjugates of general formula (X), or of schematic formula (X/a), prepared according to Claim 14, as to a polycation, additional $[(-)Ax_n]$ enhancer molecules of anionic character which may either be identical ones or of (two or more i.e. "x") different kind, are conjugated by ionic bonds, and in these bioconjugates

$$[(k/i)Mx] = [Ex_1]_{p1} + \{[(-)Cx_1]_{p2} \cdot [(+)Kx_1]_{z2}\} \cdot [(-)Ax_1]_{\text{or}} \\ [Cx_{ck} - Ex_{ck}]_{p3} + \{[(-)Cx_1]_{p2} \cdot [(+)Kx_1]_{z2}\} \cdot [(-)Ax_1]_{\text{or}} \\ [Ex_1]_{p1} + [Cx_{ck} - Ex_{ck}]_{p3} + \{[(-)Cx_1]_{p2} \cdot [(+)Kx_1]_{z2}\} \cdot [(-)Ax_1]_{\text{or}}$$

and the polycation bioconjugates are being described by the general formula (XI), or by the schematic formula (XI/a):



wherein:

"[(-)Ax _e] ₁ "	has the same meaning as in general formula (VI),
"[(-)Cx _j] _{p2} - [(+)Kx _a] _z "	has the same meaning as in general formula (VII),
"[Ex _i] _{p1} "	has the same meaning as in general formula (II),
"[Cx _d -Ix _{ck}] _{p3} "	has the same meaning as in general formula (IV),
"[(k/i)Mx] ₁ ", "m", "r"	have the same meaning as in general formula (I), further
"p ₁ ", "+"p ₃ , "+"t"+"z"	> 0 and ≤ 100, and from among
"p ₁ " and "p ₃ "	the value of at least one > 0; and
"t"	> 0,
"z" = "p ₂ "	> 0."

16) Polycation bioconjugates, according to Claim 1, characterized in that in case the enhancer molecules conjugated to the suitably selected carrier molecule of general formula (Ia) themselves are not *ab ovo* possessing the wanted (eg. antiproliferative) activity, then as a consequence of their conjugation, they will boost the originally existing biological activity of the carrier molecule.

APR 24 AMDT
17) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that each of them contains carrier molecules of general formula (IIa), molecules which may either be identical ones or of (two or more i.e. "x") different kind, having direct therapeutic effects against particular diseases, and the type of the biological activities of the polycation bioconjugates is determined by these conjugated enhancer molecules, whereas the bioavailability of the enhancer molecules is increased, due to the conjugation, so the polycation bioconjugates are more successfully applicable for treating such diseases than the particular enhancer molecules alone.

18). Polycation bioconjugates of general formula (I), according to Claim 17 characterized in that further enhancer molecules are additionally conjugated, which may either be identical ones or of (two or more i.e. "x") different kind, having affinity to particular molecules of cells/tissues/organs of the mammal organism, generating this way a selectivity or increasing the selectivity of the polycation bioconjugates towards certain target cells/tissues/organs.

19) Polycation bioconjugates of general formula (I), according to Claims 17 or 18 characterized in that they are more favourably applicable for the treatment of malignant tumors or infections, than the particular unconjugated enhancer molecules alone, from which the polycation bioconjugates are composed of

20) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that to a suitably selected given representative of the containing carrier molecules of general formula (IIa), as to a polycation, suitably selected nucleic acids - being a polyanion - is linked by ionic bonds, and therefore the polycation bioconjugate is becoming appropriate for gene transfer.

21) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that to a given representative of containing carrier molecules of general formula (IIa), certain paramagnetic contrast materials are conjugated, and additional enhancer molecules, that are capable of being selectively enriched in organs, tissues, or pathological changes (e.g. tumors) to be investigated, whereby the diagnostic value of nuclear magnetic resonance (NMR) imaging is improving.

22) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they are being introduced into the target organism on transdermal route via iontophoresis.

23) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they are capable of being appropriately incorporated into liposomes.

24) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that these are being formulated in pharmaceutically acceptable forms, and the pharmaceutical prepares so obtained, are applicable perorally, or parenterally, or transdermally, for systemic or topical use.